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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,415	07/02/2001	James D. Talton	5853-186US	7896

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EXAMINER	
SHEIKH, HUMERA N	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 06/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/856,415	TALTON ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-44 and 48-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28, 30-44 and 48-67* is/are rejected.

7)☒ Claim(s) *29* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Request for Continued Examination (RCE) under 37 C.F.R. 1.114, Applicant's Arguments/Remarks, the Rule 1.132 Declaration and the request for extension of time (1 month-granted), all filed 03/15/05 is acknowledged.

The non-statutory Double Patenting rejection of claims 68-70 has been withdrawn in view of the cancellation of claims 68-70.

Claims 28-44 and 48-67 are pending. No claims have been amended. Claims 68-70 have been cancelled. Claims 28-44 and 48-67 are rejected.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 03/15/05 has been entered.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 28, 30-44, 48, 50-54 and 59-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moro *et al.* (U.S. Pat. No. 5,223,244) in view of Green *et al.* (US Pat. No. 5,976,577).

Moro *et al.* teach aerosol compositions comprising at least one propellant, a solvent and a composite powder, whereby a sheath powder, having a particle size of 1/5 or less of a core powder is attached to the core powder that has an average particle size of 0.1 to 100 μm to form a composite powder (see reference column 2, lines 12-44); (col. 4, lines 26-37). The amount of the composite powder is preferably 0.1% to 30% by weight in the total amount of the aerosol composition (col. 5, lines 46-53). In Example 10, at column 14, lines 6-24, Moro et al. demonstrate the teaching of a powder spray, which comprises an aerosol spray that contains an active ingredient potassium glycyrrhizinate. The composite powder is granular tetrafluoroethylene (1 μm) with a kaolin coating thickness of 0.1 μm. After components (1) to (5) were mixed, the mixture was filled in an aerosol can, followed by filling components (6) and (7) to obtain a powder spray. The spray was found to have a good powder dispersibility and usability.

According to Moro et al., as the core powder of the composite powder usable, is any desired organic powder with a density of 0.7 to 2.0 and an average particle size of 0.1 to 100 μm can be used, and the powder used for the core can be in the form of a spheroid, plate, granule or needle (col. 2, lines 12-19). Moro et al. teach at column 4, lines 35-37, teach that the core powder is substantially completely covered by the coating powder and with a superior stability against separation. As the method of preparing the composite powder, the composite powder can

be prepared by mixing the core powder and the sheath powder by the dry process or the wet process (col. 3, lines 33-37).

Moro et al. are deficient in the sense that they do not explicitly teach that the coating layer is a continuous and non-porous layer. It is the Examiner's position that there is no criticality observed in the use of Applicant's continuous or non-porous layer since the instant specification permits the use of both a continuous and discontinuous coating layer (see specification pgs. 2 and 5, lines 29-32). Furthermore, it is deemed obvious to one of ordinary skill in the art to employ a continuous and non-porous coating layer to obtain a sustained or controlled rate of delivery of the active ingredient. Such skill is also evident from the reference of Green *et al.* (see below).

Green *et al.* teach a process for preparing rapidly disintegrating solid dosage forms containing drug particles, wherein the drug particles may be *coated or uncoated* with a water-insoluble polymer or lipid material, resulting in a dosage form that exhibits delayed release of the drug for a sufficient period of time to provide for controlled or *sustained release* of the drug after swallowing. The drug particles have a size such that the coatings can be formed thereon which are sufficiently *intact and continuous* to prevent or minimize loss of drug during processing. The coarse drug particles have an average particle size up to about 500 μm. In this size range, it is possible to apply a *uniform intact coating* on the particle in order to achieve efficient freeze-dried dosage forms with slow drug release rate (see reference cols. 1, line 5 – col. 3, line 22); (col. 5, lines 1-47).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the combined teachings of Moro *et al.* and Green *et al.* because Moro *et al.* teach an active ingredient formulation (i.e., glycyrrhizinate) whereby a core powder is coated and covered by a sheath powder and similarly Green *et al.* teach a dosage form comprising drug particles that are either coated or uncoated and if coated, provide a continuous intact coating on the drug particles in order to provide a sustained release of the active ingredient. The expected result would be a continuously coated, non-porous pharmaceutical formulation that exhibits a sustained release of the active drug material, as similarly desired by the Applicant(s).

Claims 28, 30-44 and 48-61 and 66-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sakon *et al.* (US Pat. No. 5,972,388) in view of Green *et al.* (US Pat. No. 5,976,577).

Sakon *et al.* teach an ultrafine particle powder for inhalation and method for the production whereby the particle powder is produced by spray-drying a mixture of active agent and a lower alkyl ether cellulose wherein the active ingredient and cellulose are either dissolved or suspended in a solution and then spray-dried into particles, whereby 80% of the particles have a particle size in the range of 0.5 to 10 μm. Particles smaller than this size do not appear to be critical since size criticality appears to depend upon administration to lower airways, which is achieved with the teachings of Sakon. Such is also the case for thickness of the coating layer. According to Sakon et al., it is desirable that the medicament is not readily removed by cilia and retained at the site to be deposited. Sustained release of the medicament while it is retained

further enhances its efficacy (col. 2, lines 35-40). Sakon et al. teach that the active ingredient includes steroids, such as triamcinolone acetonide and flunisolide, antiallergics, chemotherapy medicaments, antitussives and bronchodilators. These medicaments may be used singly, or as a mixture of two or more thereof unless the mixture is incompatible (col. 9, lines 10-26).

Sakon *et al.* do not teach that the coating layer is a continuous and non-porous layer. It is the Examiner's position that there is no criticality observed in the use of Applicant's continuous or non-porous layer since the instant specification permits the use of both a continuous and discontinuous coating layer (see specification pgs. 2 and 5, lines 29-32). Furthermore, it is deemed obvious to one of ordinary skill in the art to employ a continuous and non-porous coating layer to obtain a sustained or controlled rate of delivery of the active ingredient. Such skill is also evident from the reference of Green *et al.* (see below).

Green *et al.* teach a process for preparing rapidly disintegrating solid dosage forms containing drug particles, wherein the drug particles may be *coated or uncoated* with a water-insoluble polymer or lipid material, resulting in a dosage form that exhibits delayed release of the drug for a sufficient period of time to provide for controlled or *sustained release* of the drug after swallowing. The drug particles have a size such that the coatings can be formed thereon which are sufficiently *intact and continuous* to prevent or minimize loss of drug during processing. The coarse drug particles have an average particle size up to about 500 μm. In this size range, it is possible to apply a *uniform intact coating* on the particle in order to achieve efficient freeze-dried dosage forms with slow drug release rate (see reference cols. 1, line 5 – col. 3, line 22); (col. 5, lines 1-47).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the combined teachings of Sakon *et al.* and Green *et al.* because Sakon *et al.* teach an ultrafine particle powder formulation comprising medicaments (i.e., triamcinolone acetonide) whereby the particle powder is produced by spray-drying a mixture of active agent and a lower alkyl ether cellulose to provide a sustained release of the medicament and similarly Green *et al.* teach a dosage form comprising drug particles that are either coated or uncoated and if coated, provide a continuous intact coating on the drug particles in order to provide a sustained release of the active ingredient. The expected result would be a continuously coated, non-porous pharmaceutical formulation that exhibits a sustained release of the active drug material, as similarly desired by the Applicant(s).

Claims 28, 30-44, 48, 59-61 and 66-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hanes *et al.* (US Pat. No. 5,855,913) in view of Green *et al.* (US Pat. No. 5,976,577).

Hanes et al. teach biodegradable aerodynamically light particles incorporating a surfactant on the surface for pulmonary drug delivery whereby the particles are produced by emulsifying active agent in a polymer, such as poly(lactic acid) or PLA; or poly(glycolic acid) or PGA, in a volatile solvent. After mixing, the mixture is spray-dried and the volatile solvent is evaporated to leave the drug particle enclosed within the polymer. The particles are taught to be as small as 2 μm and can also have a mean diameter of between 5 μm and 30 μm. Particles smaller than 2 μm do not appear to be critical since size criticality appears to depend upon administration to lower airways, which is achieved with Hanes et al. Such is also the case for the

thickness of the coating layer (see reference col. 5, line 16 – col. 8, line 56) and Abstract. Hanes et al. teach that the aerodynamically light particles are highly suitable for inhalation therapies, particularly in controlled release applications (col. 8, lines 54-56). Various therapeutic agents may be employed in the formulation, including antibiotics and anti-asthmatic agents (col. 10, lines 3-49).

Hanes et al. do not explicitly teach that the coating layer is a continuous and non-porous layer. It is the Examiner's position that there is no criticality observed in the use of Applicant's continuous or non-porous layer since the instant specification permits the use of both a continuous and discontinuous coating layer (see specification pgs. 2 and 5, lines 29-32). Furthermore, it is deemed obvious to one of ordinary skill in the art to employ a continuous and non-porous coating layer to obtain a sustained or controlled rate of delivery of the active ingredient. Such skill is also evident from the reference of Green *et al.* (see below).

Green *et al.* teach a process for preparing rapidly disintegrating solid dosage forms containing drug particles, wherein the drug particles may be *coated or uncoated* with a water-insoluble polymer or lipid material, resulting in a dosage form that exhibits delayed release of the drug for a sufficient period of time to provide for controlled or *sustained release* of the drug after swallowing. The drug particles have a size such that the coatings can be formed thereon which are sufficiently *intact and continuous* to prevent or minimize loss of drug during processing. The coarse drug particles have an average particle size up to about 500 μm. In this size range, it is possible to apply a *uniform intact coating* on the particle in order to achieve efficient freeze-

dried dosage forms with slow drug release rate (see reference cols. 1, line 5 – col. 3, line 22); (col. 5, lines 1-47).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the combined teachings of Hanes *et al.* and Green *et al.* because Hanes *et al.* teach aerodynamically light drug particles contained within biodegradable polymers that provide for controlled release of the active ingredient for use in pulmonary drug delivery and similarly Green *et al.* teach a dosage form comprising drug particles that are either coated or uncoated and if coated, provide a continuous intact coating on the drug particles in order to provide a sustained release of the active ingredient. The expected result would be a continuously coated, non-porous pharmaceutical formulation that exhibits a sustained release of the active drug material, as similarly desired by the Applicant(s).

Claims 62-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moro *et al.* (US Pat. No. 5,223,244) or Sakon *et al.* (US Pat. No. 5,972,388) or Hanes *et al.* (US Pat. No. 5,855,913) in view of Bucks *et al.* (US Pat. No. 6,277,364).

The teachings of Moro *et al.* ('244), Sakon *et al.* ('388) and Hanes *et al.* ('913) have been discussed above. Moro *et al.*, Sakon *et al.* and Hanes *et al.* do not teach the inclusion of a kit having instructions.

Bucks *et al.* ('364) teach aerosol formulations that include kits and packages that comprise labeling instructions for application of the composition for the protection of skin. The labeling instructions include directions on the amount and frequency of application, methods of

removal, suggested storage conditions, shelf life expectancy, precautions or contraindications, and so forth (see reference column 5, line 65 – col. 6, line 7); (claim 4).

Therefore, it would have been obvious for one of ordinary skill in the art at the time the invention was made to use the combined teachings of either Moro et al., Sakon *et al.* or Hanes *et al.* with Bucks *et al.* because Moro et al., Sakon et al. and Hanes et al. all teach powder formulations in aerosol formulations and similarly Bucks *et al.* teach aerosol formulations that also include kits and packages comprising specific instructions (i.e., method of use, storage conditions, shelf-life extent) for the medicament. The expected result would be effective kit or packaged aerosol formulations that provide for ease and safety of usability.

Allowable Subject Matter

Claim 29 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Response to Arguments

Applicant's arguments filed 03/15/05 have been fully considered but they are not persuasive.

Applicant argued the following:

- Porous coatings, such as inherently resulting from solvent evaporation in spray processing when used to form nanoscale coatings as claimed by Applicants, clearly cannot provide sustained release profiles.
- Green discloses 'controlled or sustained release after swallowing'. Green is not combinable with Moro, Sakon and Haynes. Green does not provide any teaching regarding how to form discrete coated drug particles as claimed by Applicants.
- Green provides evidence that core particles obtained using known techniques must be at least 75 μm, more usually in the region of about 100-300 μm, to achieve a 'uniform intact coating on the particle' to achieve 'efficient freeze-dried dosage forms with slow drug release rate.
- The laser ablation method for coating drug particles is novel. Known spray-drying processes used by all cited references cannot provide Applicant's claimed nanoscale thick (1 to 500 nm) coated drug particles (< 50 μm in diameter) made possible by the laser ablation technology disclosed in the application. The Declaration provides sworn testimony that 'spray drying cannot form a plurality of coated particles as it instead forms a *porous continuous phase* having a plurality of core particles therein'.

These arguments have been thoroughly considered, but were not found persuasive. Applicant's argument that 'Green does not provide any teaching regarding how to form discrete coated drug particles as claimed by Applicants' is not persuasive since Green was relied upon for solely for the teaching of the obviousness of employing coatings that can be formed thereon

which are sufficiently intact and continuous to prevent or minimize loss of drug during processing. With regards to Applicant's argument that the thin coatings of the instant product are achieved using a 'laser ablation' process, the Examiner notes that the instant product claims are not 'product by process' claims. With regards to the Declaration, the Declaration does not establish or present evidence that the 'less than 50 μm' constitutes a critical maximum upper limitation as to provide unexpected results over the prior art without presentation of scientific data that a non-porous continuous layer could not be formed. The Declaration fails to demonstrate that the instant process is the only way to make thin coatings as claimed by Applicant. It is the position of the Examiner that whether or not the prior art can in fact form the product claimed, is not an argument that can overcome the obvious teaching of the combining of the prior art. Sufficient motivation has been provided to establish obviousness. Moreover, it is not necessary that the prior art in fact results in Applicant's claimed product, since the prior art suggests how to make a continuous coating on the particles. One of ordinary skill in the art would discern through routine experimentation how to coat drug particles having an average size of less than 50 μm. Furthermore, the Declaration is not directed to specific formulations that evidence the improved results claimed. For the reasons advanced above, Applicant's arguments were not found persuasive. The instant invention remains unpatentable over the cited art of record.

Conclusion

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.129(a) and could have been finally rejected on the grounds and

art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.129(a). Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the submission under 37 CFR 1.129(a). See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday through Friday from 8:00A.M. to 5:30P.M., alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

H. N. Sheikh H.N.S.

Patent Examiner

Art Unit 1615

May 31, 2005

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